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Lindfors, Matias

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ORIGINAL ARTICLE - BRAIN TRAUMA

Temporal changes in outcome following intensive care unit treatment after traumatic brain injury: a 17-year experience in a large academic neurosurgical centre

Matias Lindfors[1] · Juho Vehviläinen[1] · Jari Siironen[1] · Riku Kivisaari[1] · Markus B. Skrifvars[2] · Rahul Raj[1]

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Abstract

Background Traumatic brain injury (TBI) is a major cause of morbidity and mortality. However, it remains undetermined whether long-term outcomes after TBI have improved over the past two decades.

Methods We conducted a retrospective analysis of consecutive TBI patients admitted to an academic neurosurgical ICU during 1999–2015. Primary outcomes of interest were 6-month all-cause mortality (available for all patients) and 6-month Glasgow Outcome Scale (GOS, available from 2005 onwards). GOS was dichotomized to favourable and unfavourable functional outcome. Temporal changes in outcome were assessed using multivariate logistic regression analysis, adjusting for age, sex, GCS motor score, pupillary light responsiveness, Marshall CT classification and major extracranial injury.

Results Altogether, 3193 patients were included. During the study period, patient age and admission Glasgow Coma Scale score increased, while the overall TBI severity did not change. Overall unadjusted 6-month mortality was 25% and overall unadjusted unfavourable outcome (2005–2015) was 44%. There was no reduction in the adjusted odds of 6-month mortality (OR 0.98; 95% CI 0.96–1.00), but the adjusted odds of favourable functional outcome significantly increased (OR 1.08; 95% CI 1.04–1.11). Subgroup analysis showed outcome improvements only in specific subgroups (conservatively treated patients, moderate-to-severe TBI patients, middle-aged patients).

Conclusions During the past two decades, mortality after significant TBI has remained largely unchanged, but the odds of favourable functional outcome have increased significantly in specific subgroups, implying an improvement in quality of care. These developments have been paralleled by notable changes in patient characteristics, emphasizing the importance of continuous epidemiological monitoring.

Keywords Traumatic brain injury · Outcome · Mortality · Epidemiology

Background

Traumatic brain injury (TBI) is a globally increasing public health issue, causing considerable morbidity, mortality and socioeconomic repercussions to persons of all ages [17, 30]. Accordingly, the last two decades have seen rigorous attempts to reduce death and disability in patients with TBI. These efforts include the development and implementation of evidence-based guidelines, centralization of care and a multitude of clinical trials [2, 3, 7, 12, 21]. However, these initiatives have been paralleled by an epidemiological shift towards an elderly population with associated comorbidities and injuries resulting from falls rather than road traffic accidents [25]. It therefore remains uncertain whether these efforts have translated into improvements in patient outcomes.

This article is part of the Topical Collection on *Brain Trauma*

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✉ Rahul Raj
rahul.raj@hus.fi

[1] Department of Neurosurgery, Helsinki University Hospital and University of Helsinki, Topeliuksenkatu 5, PB 266, 00029 HUS Helsinki, Finland

[2] Department of Emergency Medicine and Services, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

An apparent lack of progress is supported by one voluminous meta-analysis including more than 140,000 patients over a time-span of nearly 150 years [28], and similar results have been derived in observational studies from both Europe and Australia [1, 11, 21]. Then again, some studies have yielded opposing results in settings where guideline-adherence has been thoroughly advocated [9, 10]. In addition, a recent paper demonstrated an improvement in both permanent disability and treatment cost-effectiveness in TBI patients treated in Finnish intensive care units (ICUs) during the last decade [24].

The aims of this study were to describe temporal changes in patient characteristics and outcomes in TBI patients admitted to the neurosurgical ICU (Neuro-ICU) of a large academic trauma centre during the last vicennial. Our hypothesis was that patient demographics have drifted towards an older population with no major change in patient outcomes.

Materials and methods

Ethical considerations

The ethics committee (Ethics Committee, Surgery) of the Hospital District of Helsinki and Uusimaa approved of the study and waived the need for informed consent (HUS 123/13/03/02/2016).

Study design and setting

In this single-centre, retrospective observational study, we investigated temporal changes in patient characteristics and outcomes in TBI patients admitted to the Neuro-ICU of an academic level I trauma centre (Töölö Hospital, Helsinki University Hospital [HUH], Helsinki, Finland) during a 17-year period (1 January 1999–31 December 2015). Our institution is one of five publicly funded university hospitals providing neurosurgical and neurointensive care in Finland, encompassing a catchment area population of nearly 2 million inhabitants (or roughly 35% of the Finnish population). In Finland, the neurosurgical and neurocritical care of TBI patients has for decades been centralized to five academic publicly funded university hospitals, providing care for all citizens irrespective of socioeconomic factors or insurance status. In Töölö Hospital, the treatment of TBI patients has followed the Brain Trauma Foundation (BTF) guidelines and their subsequent revisions since their introduction in 1996.

The study was conducted in agreement with the STROBE recommendations (Supplemental Digital Content 1).

Study population and data collection

We included all consecutive adult (≥ 16 years) blunt TBI patients admitted to the Neuro-ICU of Töölö Hospital between 1 January 1999 and 31 December 2015. We screened the Neuro-ICU records for patients with an ICD-10 (International Classification of Diseases and Related Health Problems, 10th Revision) diagnosis of S06.1–S06.9. All suitable patients' medical records and radiological imaging studies were reviewed to confirm the TBI diagnosis. Patients with subacute (admission > 24 h after injury) injuries, re-admissions and patients that received their primary neurosurgical treatment at another institution were not considered. We further excluded patients with penetrating TBI, and patients with either normal or missing head computed tomography (CT) scans (Fig. 1).

We extracted data regarding details on patient demographics, cause of injury, admission characteristics, extent or lack of extracranial injury, delivered treatment interventions and length of both ICU and hospital stay. Glasgow Coma Scale (GCS) score and pupillary light responsiveness were assessed at emergency department (ED) admission or prior to intubation for sedated patients. Major extracranial injury was defined as an injury necessitating hospital admission on its own (according to the CRASH-TBI criteria) [29]. Moreover, admission head CT scans were retrieved from the Picture Archiving and Communicating System (PACS) registry and classified according to the Marshall CT classification [18]. Evacuated and non-evacuated mass lesions were, however, combined into one category, as the distinction between the two is arbitrary [14, 20, 23].

Patients who underwent a craniotomy or decompressive craniectomy were categorized as operatively admitted, whereas patients who underwent no such operation were classified as conservatively admitted. Furthermore, patients who underwent decompressive craniectomy were divided into two groups according to timing of the operation into early decompressive craniectomy (performed within 48 h of admission) and late decompressive craniectomy (performed after 48 h of admission). If the patient first underwent craniotomy and hematoma evacuation, where after a decompressive craniectomy was performed, the patient was put in the late decompressive craniectomy group.

Outcome variables

Our primary outcomes of interest were 6-month all-cause mortality and Glasgow Outcome Scale (GOS) closest to 6-month follow-up. We also report 30-day all-cause mortality. Dates of death were extracted from the Population Register Centre of Finland (available for all Finnish residents) and GOS scores were adjudicated retrospectively from the patients' medical records. GOS assessment was possible from 2005 onwards (use of electronic health care records started), and median time to GOS follow-up for 6-month survivors was 5 months (IQR 2–8 months). For the statistical analyses, GOS

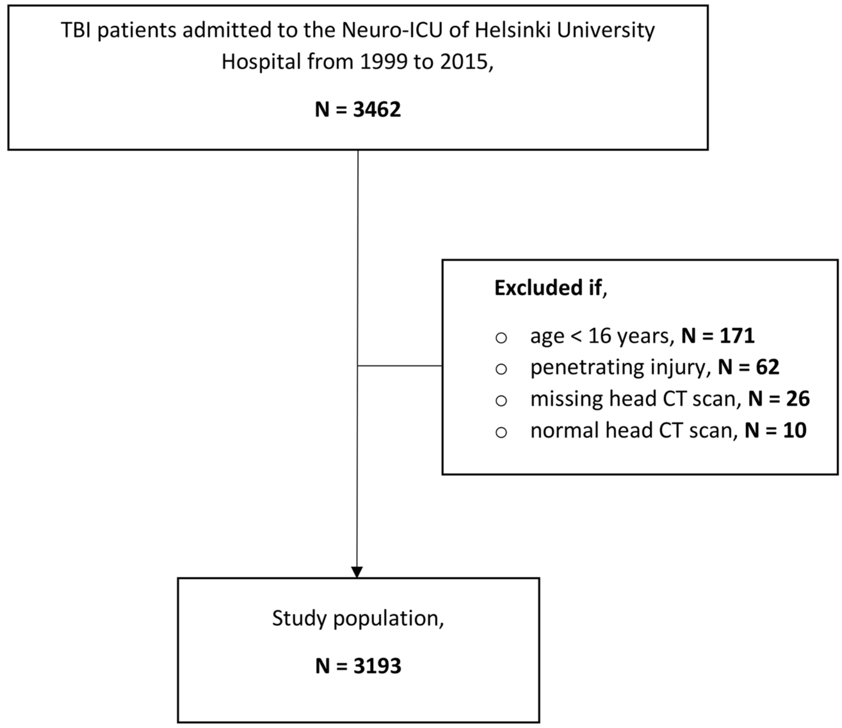

Fig. 1 Flow chart presenting the inclusion and exclusion of patients. TBI traumatic brain injury, Neuro-ICU neurosurgical intensive care unit

was further dichotomized to favourable outcome (GOS 4–5) and unfavourable outcome (1–3).

Statistical analysis

All statistical analyses were performed with the use of SPSS Statistics for Windows, version 24.0, released 2016 (IBM Corp, Armonk, NY, USA).

Descriptive data are presented as absolute numbers and percentages for categorical variables and as medians and interquartile ranges for continuous variables. Categorical data were analysed using the χ^2 test (two-tailed). Continuous data were tested for skewness; all data were highly skewed and hence analysed using the Mann-Whitney *U* test.

Temporal changes in 6-month mortality and functional outcome (GOS) were assessed using multivariate logistic regression analysis, adjusting for TBI severity (case-mix) and using year of admission as a continuous variable. A TBI severity model including age, sex, GCS motor score, pupillary light responsiveness, Marshall CT classification and major extracranial injury was built using multivariate logistic regression modelling. The pre-defined subgroups were separately analysed. These subgroups were moderate-to-severe TBI (GCS 3–12), mild TBI (GCS 13–15), operative admission, conservative admission, young patients (16–40 years), middle-aged patients (41–64 years), old patients (≥ 65 years) and very old patients (≥ 75 years). We also calculated risk-adjusted mortality rates (RAMR) and risk-adjusted disability rates (RADR). The RAMR and RADR are calculated as the ratio between the observed and the predicted outcome multiplied by the overall outcome rate. Thus, the RAMR and RADR represent the estimated outcome if TBI severity (variables described above) had remained the same throughout the study period.

Missing baseline data (motor score [$N = 57$] and pupillary light responsiveness [$N = 42$]) were substituted using logistic regression multiple imputation (fully conditional specification, 10 iterations, imputating motor score and pupillary light responsiveness based on age, Marshall CT classification, admission type, requirement of mechanical ventilation, length of ICU stay and 30-day mortality) prior to multivariate analyses, thus utilizing all available outcome data.

The results are presented as odds ratios (OR) with 95% confidence intervals (CI). p values < 0.05 are considered statistically significant.

Results

Baseline characteristics

The study population consisted of 3193 patients. Patient baseline characteristics are presented in Table 1. Patient median age was 54 years, and males represented 76% of all patients. Falls from ground level accounted for more than half of all injuries and were more typical in elderly patients (Supplemental Digital Content 2). Fifty-seven percent of patients had an admission GCS score of 3–12, and 53% had a large mass lesion on their admission head CT scan. Higher GCS scores and more large mass lesions were noted among

Table 1 Patient baseline characteristics

Variable	All patients ($N = 3193$)	6-month survivors ($N = 2389$)	6-month non-survivors ($N = 804$)	p value
Age	54 (42–66)	52 (39–63)	61 (50–70)	< 0.001
Sex				
Male	2421 (76%)	1808 (76%)	613 (76%)	0.747
Female	772 (24%)	581 (24%)	191 (24%)	
Cause of injury				
Fall from ground level	1836 (58%)	1310 (55%)	526 (65%)	< 0.001
Fall from height	251 (8%)	195 (8%)	56 (7%)	
Road traffic accident	447 (14%)	374 (16%)	73 (9%)	
Interpersonal violence	201 (6%)	181 (8%)	20 (2%)	
Other	76 (2%)	64 (3%)	12 (1%)	
Unknown	382 (12%)	265 (11%)	117 (15%)	
GCS score				
3–8	1256 (39%)	775 (32%)	481 (60%)	< 0.001
9–12	559 (18%)	461 (19%)	98 (12%)	
13–15	1090 (34%)	939 (39%)	151 (19%)	
Missing	288 (9%)	214 (9%)	74 (9%)	
GCS motor scale				
1	556 (17%)	290 (12%)	266 (33%)	< 0.001
2	115 (4%)	57 (2%)	58 (7%)	
3	41 (1%)	20 (1%)	21 (3%)	
4	340 (11%)	228 (10%)	112 (14%)	
5	907 (28%)	744 (31%)	163 (20%)	
6	1177 (37%)	1009 (42%)	168 (21%)	
Missing	57 (2%)	41 (2%)	16 (2%)	
Pupil responsiveness				
None	329 (10%)	117 (5%)	212 (26%)	< 0.001
One	396 (12%)	250 (10%)	146 (18%)	
Both	2426 (76%)	1991 (83%)	435 (54%)	
Missing	42 (1%)	31 (1%)	11 (1%)	
Major extracranial injury	377 (12%)	283 (12%)	94 (12%)	0.907
Marshall CT classification				
Diffuse injury II	1069 (34%)	936 (39%)	133 (17%)	< 0.001
Diffuse injury III	272 (9%)	185 (8%)	87 (11%)	
Diffuse injury IV	157 (5%)	114 (5%)	43 (5%)	
Evacuated or non-evacuated mass lesion	1695 (53%)	1154 (48%)	541 (67%)	
Admission type				
Operative	1862 (58%)	1365 (57%)	497 (62%)	0.020
Conservative	1331 (42%)	1024 (43%)	307 (38%)	
Operation type				
Craniotomy and hematoma evacuation	1749 (55%)	1301 (54%)	448 (56%)	< 0.001
Decompressive craniectomy	113 (4%)	64 (3%)	49 (6%)	
Late decompressive craniectomy	43 (1%)	34 (1%)	9 (1%)	0.518
Mechanical ventilation	2569 (81%)	1822 (76%)	747 (93%)	< 0.001
ICP-monitoring	680 (21%)	477 (20%)	203 (25%)	0.002
External ventricular drain	169 (5%)	107 (4%)	62 (8%)	< 0.001
Length of intensive care unit stay (days)	3 (1–6)	3 (1–6)	2 (1–5)	< 0.001
Length of hospital stay (days)	8 (4–14)	9 (5–14)	6 (2–12)	< 0.001

Categorical variables shown as N (%) and continuous variables shown as median (IQR)

CT computerized tomography, *ICP* intracranial pressure, *GCS* Glasgow Coma Scale

older patients (Supplemental Digital Content 2). Patients with admission GCS scores of 13–15 were older than patients with admission GCS scores of 3–12 (Supplemental Digital Content 3). Still, half of patients with an admission GCS score of 13–15 underwent craniotomy or decompressive craniectomy. In total, 58% percent were operatively treated of which 94% were treated by craniotomy and 6% by decompressive craniectomy. Of all patients, 21% were ICP monitored, but of all patients with severe (GCS ≤ 8) injury, 36% were ICP monitored. External ventricular drainage was employed in 5%

of patients. Older patients underwent more often craniotomy and hematoma evacuation but were more seldom ICP monitored than younger patients. Only three decompressive craniectomies were performed in patients 65 years or older. Median ICU length of stay was 3 days (IQR 1–6) and median hospital length of stay was 8 days (IQR 4–14).

Unadjusted outcomes

Overall unadjusted 30-day and 6-month mortality were 19 and 25%, respectively. Patients alive 6 months post-injury were younger, were more likely to be injured in road traffic accidents instead of ground level falls, had less severe injuries and were less likely to undergo craniotomy or decompressive craniectomy than 6-month non-survivors (Table 1). Six-month mortality varied between 19 and 31% over the study period. GOS scores were available for 95% ($N = 2058/2159$) of patients admitted from 2005 onwards; unfavourable outcome was present in 44% ($N = 909/2058$) of all patients and in 24% ($N = 370/1519$) of 6-month survivors (Fig. 2). Total unfavourable outcome varied within 35% and 55% during 2005–2015. GOS scores were missing for 10–12% of patients during 2005–2007, for 7% of patients during 2008–2009 and for 0–1% of patients during 2010–2015.

Temporal changes in patient characteristics

Patient median age increased from 51 years in 1999 to 60 years in 2015 (Supplemental Digital Content 4). Falls from ground level as mechanisms of injury became more frequent over the course of the study period (increasing from 46% in 1999 to 60% in 2015). In 1999, only 22% of patients had an admission GCS score of 13–15, in comparison to 53% in 2015. The proportion of Marshall diffuse injury types 3 and 4 decreased during the study period, while large mass lesions became more common. The percentage of patients undergoing craniotomy or decompressive craniectomy decreased from 74% in 1999 to 42% in 2015. Also, the sum rate of ICP monitoring and external ventricular drainage decreased from 1999 to 2015. Still, TBI overall severity (model including age, sex, GCS motor score, pupillary light responsiveness, Marshall CT classification and major extracranial injury) remained unchanged during the study period (Supplemental Digital Content 5).

Temporal changes in mortality

All patients were included in the mortality analyses. The TBI severity adjusted odds of death did not decrease significantly for neither 6-month mortality (OR 0.98, 95% CI 0.96–1.00) nor 30-day mortality (OR 0.98, CI 95% 0.96–1.01) over the observed study period. Subgroup analysis is presented in Table 2. Of the pre-defined subgroups, only patients treated conservatively showed a lowered risk for mortality (OR 0.94, 95% CI 0.91–0.98). RAMR decreased from 33% (95% CI 24–41%) in 1999 to 25% (95% CI 19–30%) in 2015 (Fig. 3).

Temporal changes in functional outcome

Patients with missing GOS data ($N = 101/2159$, 4.7%, during 2005–2015) were not included in the functional outcome analyses. There was a statistically significant increase in the TBI severity adjusted odds of favourable functional outcome for every increasing admission year (OR 1.08, 95% CI 1.04–1.11, $p < 0.001$). In the subgroup analysis, the change was significant only in the middle-aged subgroup (OR 1.10, 95% CI 1.05–1.16), the moderate-to-severe TBI subgroup (OR 1.08, 95%

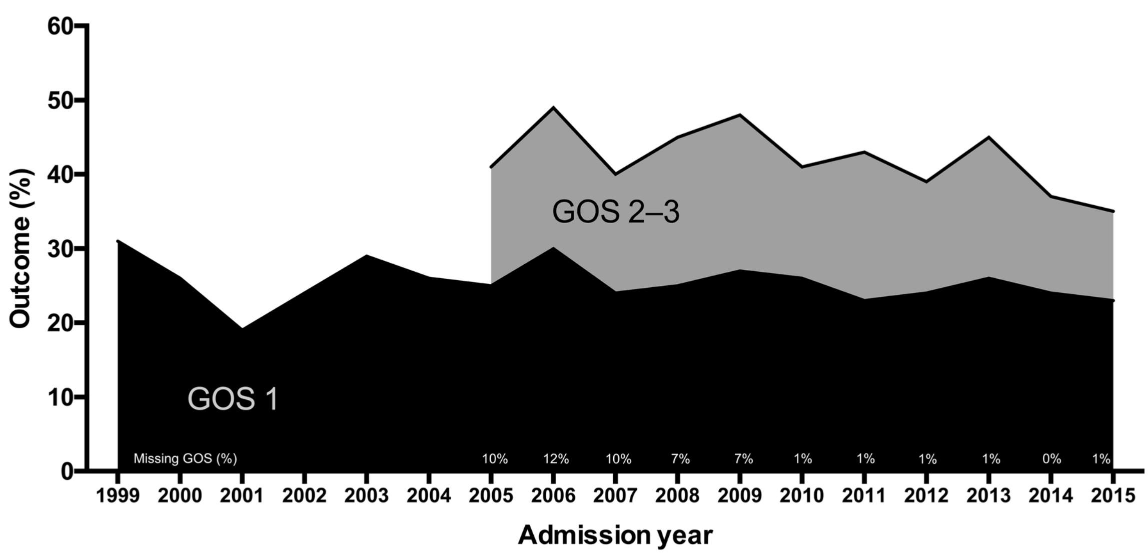

Fig. 2 Temporal changes in unadjusted 6-month mortality (GOS 1) and unfavourable functional outcome (GOS 2–3). Mean unadjusted 6-month mortality was 25% and varied from 19 to 31% during 1999–2015. Mean unadjusted 6-month unfavourable functional outcome was 44% and varied from 35 to 55% during 2005–2015. Functional outcome (GOS) was assessed from 2005 onwards. GOS Glasgow Outcome Scale

Table 2 Subgroup analysis for temporal changes in 6-month mortality and 30-day mortality

Subgroup	OR	95% CI	*p* value
Mean annual change in risk of 6-month mortality			
Overall	0.98	0.96–1.00	0.079
GCS subgroups			
3–12	0.98	0.96–1.01	0.113
13–15	1.01	0.97–1.05	0.763
Age subgroups			
16–40	1.00	0.94–1.06	0.928
41–64	0.99	0.96–1.02	0.419
≥ 65	0.98	0.95–1.01	0.147
≥ 75	0.96	0.91–1.01	0.153
Admission type subgroups			
Operative	0.99	0.97–1.02	0.589
Conservative	0.94	0.91–0.98	0.002
Subgroup	OR	95% CI	*p* value
Mean annual change in risk of 30-day mortality			
Overall	0.98	0.96–1.01	0.132
GCS subgroups			
3–12	0.99	0.96–1.02	0.411
13–15	0.99	0.94–1.04	0.676
Age subgroups			
16–40	1.00	0.93–1.07	0.983
41–64	0.99	0.96–1.03	0.728
≥ 65	0.97	0.94–1.00	0.083
≥ 75	0.96	0.91–1.02	0.172
Admission type subgroups			
Operative	0.99	0.96–1.02	0.366
Conservative	0.92	0.88–0.96	< 0.001

All analyses were logistic regression analyses adjusting for age, sex, GCS motor score, pupillary light responsiveness, Marshall CT classification, major extracranial injury, and using year of admission as a continuous variable. An OR over 1 indicates that the risk for death increases with every increasing admission year. An OR under 1 indicated that the risk for death decreases with every increasing admission year

GCS Glasgow Coma Scale, *OR* odds ratio, *CI* confidence interval

CI 1.03–1.14) and the conservatively admitted subgroup (OR 1.13, 95% CI 1.07–1.19) (Table 3). A trend towards improved outcome was noted for young patients ($p = .056$) and operatively admitted patients ($p = .062$), although it did not reach statistical significance. RADR decreased from 47% (95% CI 40–55%) in 2005 to 39% (95% CI 32–45%) in 2015 (Fig. 3).

Discussion

Key findings

In this comprehensive observational study including more than 3000 patients and spanning nearly two decades, we investigated temporal changes in the characteristics and outcomes of patients with a TBI requiring ICU treatment. We noted no overall reduction in TBI severity adjusted 6-month mortality or 30-day mortality. However, subgroup analysis showed a statistically significant reduction in mortality for conservatively treated patients. An overall improvement in functional outcome was observed from 2005 to 2015. Subgroup analysis revealed that this improvement in functional outcome occurred in conservatively admitted patients, middle-aged patients and in patients with moderate-to-severe TBI. These changes were paralleled by a notable change in patient characteristics towards more elderly patients with higher admission GCS scores. Still, overall TBI severity did not change during the study period, implying that the quality of care has improved.

Our findings are largely compatible with those of previous studies from across the developed world, where ageing populations and advances in road safety have led to a change in TBI patient characteristics towards more ground level falls in the elderly and a concomitant decrease in the proportion of motor vehicle accidents, the latter often associated with young and more severely injured patients [25]. We observed ground level falls to represent a considerable proportion of all mechanisms of injury, an observation typical to the Nordic countries [22]. These findings are most likely explained by a relatively old and ageing population, although behavioural factors such as patterns of alcohol consumption are probably involved as well [26]. The increase in the proportion of mild TBIs is likewise probably related to changes in patient demographics and causes of injury. It should, however, be highlighted that these are not purely mild TBIs as all patients were treated in the ICU due to their TBI and approximately half underwent craniotomy or decompressive craniectomy, half had a large mass lesion and two-thirds were mechanically ventilated. Furthermore, a recent study suggests that GCS may be a suboptimal tool in classifying the degree of injury in elderly patients, grading them less severe than their anatomical counterparts in younger individuals [13]. Thus, the noted parallel increase in age and admission GCS scores did not affect overall TBI severity, which remained largely constant during the study period (Supplemental Digital Content 5).

Changes in patient characteristics are partly due to an increase in ICU beds and have, hence, resulted in concomitant changes in treatment. The steady decrease in the proportion of patients whose injuries necessitated mechanical ventilation or ICP-monitoring is consistent with the observed increases in patient age and admission GCS scores. The reduction in ICP monitoring is further compatible with the decrease in the proportion of patients with injuries categorized as Marshall types 3 and 4, a finding presumably explained by the fact that elderly patients are more likely to have cerebral atrophy allowing larger mass lesions to form before a clinically significant increase in ICP [5, 6]. Furthermore, we observed a declining rate

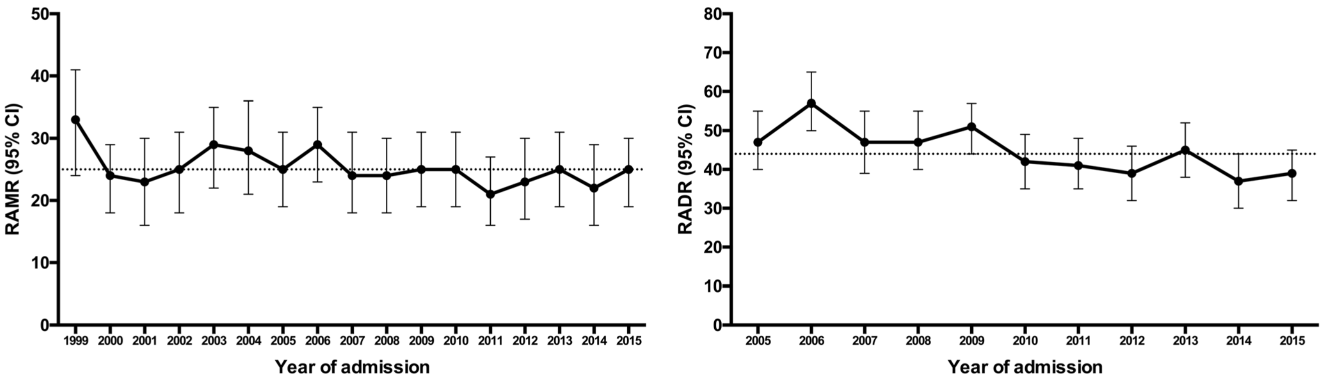

Fig. 3 Temporal changes in 6-month risk-adjusted mortality rate (RAMR, to the left) and risk-adjusted disability rate (RADR, to the right). The RAMR represents the estimated 6-month mortality rate with a constant TBI severity. The RADR represents the estimated 6-month disability rate with a constant TBI severity. The RAMR decreased from 33% (95% CI 24–41%) in 1999 to 25% (95% CI 19–30%) in 2015, but the reduction was not statistically significant ($p = 0.079$). The RADR decreased from 47% (95% CI 40–55%) in 2005 to 39% (95% CI 32–45%) in 2015. An increase in admission year was significantly associated with an increased risk for favourable functional outcome (odds ratio 1.08; 95% CI 1.04–1.11). Functional outcome (GOS) was assessed from 2005 onwards. GOS was dichotomized to favourable (GOS 4–5) and unfavourable (GOS 1–3) functional outcome. GOS Glasgow Outcome Scale

of neurosurgical interventions (craniotomy or decompressive craniectomy, ICP monitoring, EVD placement) although the proportion of patients presenting with significant mass lesions increased. It should, however, be highlighted that the definition of significant mass lesion according to the Marshall CT classification [18] is any intracranial bleeding 25 cc or larger, which might include thin acute subdural hematomas or deep traumatic parenchymal haemorrhages not necessarily requiring evacuation. Although we cannot establish a causal relationship, it is possible that the noticed improvement in outcome for conservatively treated patients is due to more aggressive and effective conservative treatment of such cases. Further, there is evidence suggesting that a more conservative approach to neurosurgical interventions does not necessarily affect patient outcome [8]. However, evaluating the effectiveness of any given treatment approach is beyond the scope of this observational report and warrants further investigation.

Table 3 Subgroup analysis for temporal changes in 6-month favourable functional outcome

Subgroup	OR	95% CI	*p* value	Missing GOS
Mean annual change in risk of 6–month favourable functional outcome				
Overall	1.08	1.04–1.11	< 0.001	101 (5%)
GCS subgroups				
3–12	1.08	1.03–1.14	0.001	43 (4%)
13–15	1.04	0.98–1.10	0.224	34 (4%)
Age subgroups				
16–40	1.10	1.00–1.22	0.056	25 (6%)
41–64	1.10	1.05–1.16	< 0.001	56 (5%)
≥ 65	1.03	0.98–1.10	0.258	20 (3%)
≥ 75	1.05	0.96–1.16	0.303	6 (2%)
Admission type subgroups				
Operative	1.05	1.00–1.09	0.062	43 (4%)
Conservative	1.13	1.07–1.19	< 0.001	58 (6%)

All analyses were logistic regression analyses adjusting for age, sex, GCS motor score, pupillary light responsiveness, Marshall CT classification, major extracranial injury, and using year of admission as a continuous variable. An OR over 1 indicates that the risk for favourable functional outcome increases with every increasing admission year. An OR under 1 indicates that the risk for favourable functional outcome decreases with every increasing admission year

GCS Glasgow Coma Scale, *OR* odds ratio, *CI* confidence interval

The stagnating trend in mortality is compatible with the lack of recent advances in the acute management of TBI [2]. Then again, it is possible that improvements in outcome are confounded by the observed change over time in patient demographics and profile of injury. Moreover, it may be that the lack of improvement is, in part, representative of the irreversible nature of the primary injury, the consequences of which remain inescapable until the development of an effective neuroprotective or neuroregenerative therapy [16]. In contrast to the lack of progress in mortality, a rather crude outcome measure, an improvement in functional outcome was observed. This was most profound in the conservatively admitted subgroup, probably reflecting the consequence of more mildly injured patients being admitted but may also suggest an improvement in the conservative treatment of TBI. However, our study setting is unable to fully disclose the true reasons behind this trend; the causes of which are probably multifactorial and necessitate a more thorough exploration in the future.

Comparison with previous studies

Previous studies investigating trends in long-term outcomes after TBI are relatively scarce. A recent study from Australia analysed data from the Victoria State Trauma Registry over the past 10 years and observed no improvement in functional outcome, with changes similar to ours in patient demographics and causes of injury [1]. Another study utilizing the TARN database yielded similar results, with no improvement in in-hospital or 30-day mortality since the early 1990s [21]. In addition, a recent analysis of a multicentre ICU database found no improvement in mortality over an 11-year study period, yet a reduction in risk-adjusted disability together with improved treatment cost-effectiveness was observed [24]. Then again, a study by Gerber and colleagues observed a significant reduction in 2-week case-fatality rate [10], and a similar trend was demonstrated in a more recent analysis of the TARN trauma registry [9]. Finally, the lack of improvement in mortality is supported by the findings from an extensive meta-analysis including more than 140,000 patients over the course of 150 years [28].

Strengths and limitations

To the best of our knowledge, this study is the largest to date to examine temporal changes in long-term outcomes following significant TBI. Among its strengths is that it was conducted within a publicly funded healthcare system in a trauma centre with a catchment area population of nearly two million people (35% of the Finnish population), over a 17-year period of investigation. Moreover, we were able to extract data on functional outcome for 95% of patients from 2005 onwards, enabling the assessment of trends in functional outcome over a period of 11 consecutive years. Furthermore, we included in our study the classification of all patients' admission head CT scans. This provided us with an additional adjustable covariate, one that is lacking in most previous studies.

Nonetheless, our study is subject to certain limitations that require acknowledgement. Firstly, the study was retrospective in nature, resulting in missing baseline and outcome data for a small subset of patients. However, the absolute amount of missing baseline data was low and substituted using multiple imputation, an approach that enabled us to make use of all available outcome data and avoid case exclusion [19]. Moreover, we conducted additional analyses using the original rather than the imputed data, which yielded similar results. We therefore consider it unlikely that any missing data would have confounded our results. Secondly, the study was conducted in a single-centre setting. Nevertheless, our institution is one of the largest tertiary trauma centres in Northern Europe and the largest neurosurgical unit in Finland. Thus, we believe that our study sample is adequately representative of all TBIs necessitating ICU treatment in Finland. Thirdly, we only included patients who had been admitted to a neurosurgical ICU. This may have excluded, for instance, elderly patients with injuries deemed not in need of neurosurgical interventions, as it is possible that such patients are less likely to be admitted for special care. However, we observed a marked increase over time in patient median age, suggesting that age itself is decreasingly important in decisions concerning ICU admission. Finally, due to the study's retrospective design and its inherent restrictions in data availability, we were compelled to assess functional outcome using GOS and at 6 months post-injury. The inability of GOS to capture impairments in cognitive function and health-related quality of life is well recognized [27], whereas the assessment of outcome 6 months after injury is unlikely to represent final recovery for all patients [4].

Implications for future research

Notwithstanding the achievements and added value of this and other studies conducted to date, the TBI research community is lacking more patient series for the continuous evaluation of trends in outcome after TBI. Moreover, as is evident in the rapidly changing patient demographics and mechanisms of injury, epidemiological monitoring remains a matter of paramount importance and necessitates standardized data collection, as has been previously advocated [15]. Future studies should focus their aims towards utilizing comparative effective research to identify effective therapies for targeted groups of patients, and to yield improvements in outcome through the development, optimization and more widespread use of individualized treatment approaches.

Conclusions

During the past two decades, mortality following significant TBI has remained largely unchanged, but an increase in the likelihood of favourable functional outcome was observed in specific subgroups, possibly suggesting an improvement in the quality of care. These developments have been paralleled by shift in patient characteristics towards older patients with higher admission GCS scores, emphasizing the importance of continuous epidemiological monitoring.

Author contribution statement RR had the main responsibility for study design, interpretation of data, and coordinating the study. ML and RR had the main responsibility in writing the manuscript. RR and ML were in charge of the statistical analyses. JV, JS, RK and MS contributed to acquisition of data, data analysis, interpretation of data and revision of the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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